

## CLAIMS

1. A method for screening compounds inhibiting signal transduction through inflammatory cytokines, the method comprising  
5 the steps of:

- (a) contacting a test sample with TAK1 and TAB1;
- (b) detecting binding between the TAK1 and the TAB1; and
- (c) selecting a compound inhibiting the binding.

2. The method of claim 1, wherein the TAK1 and/or the TAB1 is  
10 fused with a peptide.

*Sub a2* 3. The method of claim 1 or 2, wherein the TAK1 or the TAB1  
is linked to a support.

4. The method of any one of claims 1 to 3, wherein a label is attached to the TAK1 or the TAB1 and wherein the binding is detected  
15 by detecting or measuring the label.

5. The method of any one of claims 1 to 3, wherein the binding is detected by detecting or measuring the TAB1 bound to the TAK1 with a primary antibody against TAB1 or a primary antibody against the peptide fused with the TAB1.

20 6. The method of any one of claims 1 to 3, wherein the binding is detected by detecting or measuring the TAK1 bound to the TAB1 with a primary antibody against TAK1 or a primary antibody against the peptide fused with the TAK1.

25 7. The method of any one of claims 1 to 3, wherein the binding is detected by detecting or measuring the TAB1 bound to the TAK1 with a primary antibody against the TAB1 or a primary antibody against the peptide fused with TAB1, and a secondary antibody against the primary antibody.

30 8. The method of any one of claims 1 to 3, wherein the binding is detected by detecting or measuring the TAK1 bound to the TAB1 with a primary antibody against TAK1 or a primary antibody against the peptide fused with the TAK1, and a secondary antibody against the primary antibody.

35 9. The method of any one of claims 5 to 8, wherein the primary antibody or the secondary antibody is labeled with radioisotope, enzyme, or fluorescent substance.

10. The method of claim 2, wherein the binding is detected with, as an index, change in the expression level of a reporter gene which is activated in response to the binding.

11. The method of claim 10, wherein the reporter gene is luciferase, chloramphenicol acetyltransferase, green fluorescent protein, or  $\beta$ -galactosidase.

12. A method for screening compounds inhibiting signal transduction through inflammatory cytokines, the method comprising the steps of:

10 (a) contacting a test sample with TAK1;

(b) detecting phosphorylation by the TAK1; and

(c) selecting a compound inhibiting the phosphorylation.

13. A method for screening compounds inhibiting signal transduction through inflammatory cytokines, the method comprising the steps of:

15 (a) contacting a test sample with TAK1 and TAB1;

(b) detecting phosphorylation by the TAK1; and

(c) selecting a compound inhibiting the phosphorylation.

Sub A3  
20 14. The method of claim 12 or 13, wherein a substrate for the TAK1 is added and wherein the phosphorylation of the substrate by the TAK1 is detected.

15. The method of claim 14, wherein the substrate for the TAK1 is MKK6 and/or MKK3.

Sub A4  
25 16. The method of any one of claims 12 to 15, wherein the TAK1 is fused with a peptide.

17. The method of any one of claims 12 to 16, wherein the TAK1 is linked to a support.

18. A method for screening compounds inhibiting signal transduction through inflammatory cytokines, the method comprising the steps of:

30 (a) introducing a test sample into and/or contacting the sample with cells expressing TAK1;

(b) detecting and/or measuring a biological activity transduced through the TAK1; and

35 (c) selecting a compound reducing the biological activity.

19. The method of claim 18, wherein the biological activity

is a biological activity of inflammatory cytokines.

20. The method of claim 18, wherein the biological activity is detected with, as an index, change in the expression level of a reporter gene which is activated in response to the activity.

5 21. A method for screening compounds inhibiting signal transduction through inflammatory cytokines, the method comprising the steps of:

(a) introducing a test sample into and/or contacting the sample with cells expressing TAK1 and TAB1;

10 (b) detecting and/or measuring a biological activity transduced through the TAK1 and the TAB1; and

(c) selecting a compound reducing the biological activity.

22. The method of claim 21, wherein the biological activity is a biological activity of IL-1 or TNF.

15 23. The method of claim 21, wherein the biological activity is detected with, as an index, change in the expression level of a reporter gene which is activated in response to the activity.

*Sub 25* 24. The method of claim 20 or 23, wherein the reporter gene is luciferase, chloramphenicol acetyltransferase, green fluorescent protein, or  $\beta$ -galactosidase.

25 25. The method of any one of claims 18 to 24, wherein an inflammatory stimulus is given to cells and wherein the biological activity transduced through TAK1 or through TAK1 and TAB1 is detected and/or measured.

26. The method of claim 25, wherein the inflammatory stimulus is IL-1, TNF, or LPS.

*Sub 26* 27. The method of any one of claims 1 to 26, wherein the inflammatory cytokine is IL-1, TNF, IL-10, or IL-6.

30 28. A compound for inhibiting signal transduction through inflammatory cytokines, the compound that can be isolated by the method of any one of claims 1 to 27.

29. A pharmaceutical composition containing as an active ingredient the compound of claim 28.

35 30. An inhibitor of the signal transduction through inflammatory cytokines, the inhibitor having an activity of inhibiting signal transduction through TAK1.

31. An inhibitor of the activity of inflammatory cytokines, the inhibitor having an activity of inhibiting signal transduction through TAK1.

5 32. An inhibitor of the production of inflammatory cytokines, the inhibitor having an activity of inhibiting signal transduction through TAK1.

10 33. A pharmaceutical composition for inhibiting signal transduction through inflammatory cytokines, the pharmaceutical composition comprising as an active ingredient a compound inhibiting signal transduction through TAK1.

34. A pharmaceutical composition for inhibiting the activity of inflammatory cytokines, the pharmaceutical composition comprising as an active ingredient a compound inhibiting signal transduction through TAK1.

15 35. A pharmaceutical composition for inhibiting the production of inflammatory cytokines, the pharmaceutical composition comprising as an active ingredient a compound inhibiting signal transduction through TAK1.

20 *Sub-a1* 36. The pharmaceutical composition of any one of claims 33 to 35, wherein the pharmaceutical composition is an anti-inflammatory agent.

37. The pharmaceutical composition of any one of claims 33 to 36, wherein the compound is a compound inhibiting binding between TAK1 and TAB1.

25 38. The pharmaceutical composition of any one of claims 33 to 36, wherein the compound is a compound inhibiting phosphorylation by TAK1.

30 39. The pharmaceutical composition of any one of claims 33 to 38, wherein the compound is a compound that can be isolated by the method of any one of claims 1 to 27.

40. The pharmaceutical composition of any one of claims 33 to 39, wherein the inflammatory cytokine is IL-1, TNF, IL-10, or IL-6.